Remarks/Arguments

The present amendment, without prejudice to future prosecution: amends claims 3, 5, 7, 24, 29 and 31; cancels claim 6; and adds new claims 33 and 34.

Claims 3, 24 and 31 were amended to further describe "consists essentially". Support for the amendment is provided in the application on page 7, third full paragraph.

Claim 5 was amended to incorporate the description provided in dependent claim 6, and to more particularly point out that the referenced naturally occurring sai-1 polypeptide.

Claim 29 was amended to delete "with".

New claims 33 and 34 ultimately depend from claim 5 and further describe the SEQ ID NO: 1 related polypeptide. Support for the polypeptide sequence is provided in the application, for example, on page 7, second paragraph.

35 U.S.C. § 101

Claims 1 and 5, and claims dependent thereon stand rejected as allegedly directed towards non-statutory subject matter. The rejection indicates that these claims read on a naturally occurring fragment of SEQ ID NO: 1. The rejection is respectfully traversed.

Claim 1 provides for less than a full-length sequence. It is respectfully submitted that the rejection fails to provide support for a particular naturally occurring fragment within the scope of claim 1 being found in nature. Instead, the rejection seems to indicate that such fragment may be present in nature.

Claim 19 is dependent on claim 1 and further describes the polypeptide as substantially purified. Claims 20-25 depend from claim 19.

Claim 5 was combined with claim 6. Claim 6 refers to a pharmaceutically acceptable carrier.

35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-3, 5-7, 19-23, and 25-31 stand rejected as allegedly lacking written description. The rejection argues that reference to "*S. aureus*" requires the polypeptide to provide protection against any *S. aureus*; and that the specification fails to identify the regions of SEQ ID NO: 1 important for providing protective immunity, which up to 15 amino acid residues within SEQ ID

NO: 1 should be altered to maintain the required biological function, or which 1% of amino acid residues within SEQ ID NO: 1 should be altered to maintain the required biological function. The rejection also argues that the data provided in the application fails to demonstrate significant protection in vaccine immunized mice compared to AHP-injected control mice. The rejection is respectfully traversed.

The present application reasonably conveys to those skilled in the art that applicants were in possession of polypeptides having a substantially similar sequence to SEQ ID NO: 1 and which provide protective immunity against *S. aureus*. The reasonable conveyance is based on the high degree of structural relationship between the SEQ ID NO: 1 related polypeptides recited in the claims.

Applicant is not required to illustrate the ability of the claimed polypeptide to provide protective immunity against each and every *S. aureus*. The data provided for SEQ ID NO: 3 illustrates that a polypeptide of SEQ ID NO: 1 is able to reproducibly provide for some protective immunity against a strain of *S. aureus*. SEQ ID NO: 3 is a His-tag version of SEQ ID NO: 1. (See the present application at page 5, paragraphs 5-7.) Figures 7A and 7B illustrate that more mice survive when immunized with a polypeptide vaccine (SEQ ID NO: 3) than with the adjuvant control.

Polypeptides having a high degree of structural similarity are expected to have similar properties. The rejection fails to take into account the structurally similarity of the polypeptides recited in the claims. Instead, the rejection is based on the possibility that an alteration to a critical amino acid within the 260 amino acids of SEQ ID NO: 1 may impact a protein antibody interaction.

The rejection fails to provide any indication as to why a significant number of polypeptides within the scope of the claims would fail to provide protection. For example, is the patent office arguing that if 1% of the alterations within SEQ ID NO: 1 disrupt an antibody polypeptide interaction that written description is lacking?

Additionally, the possibility that some unknown alteration in an amino acid residue may impact a particular protein antibody interaction, does not necessarily equate to a polypeptide within the scope of claims not providing protective immunity. For example, SEQ ID NO: 1 is 260 amino acids in length and may contain more than one epitope providing a beneficial effect.

It is respectfully submitted that SEQ ID NO: 1 is sufficiently representative of polypeptides described in the claims. The claims provide for varying high degrees of structural similarity ranging from SEQ ID NO: 1 to sequences with 1-15 amino acid alterations from SEQ ID NO:. 1.

The described high degree of structural relationship to SEQ ID NO: 1 provides more than a mere wish for obtaining a compound able to provide protective immunity. It provides a representative polypeptide and an expectation that polypeptides having a similar structure would have similar properties. To meet the written description requirement "applicant must . . . convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention." In re Alton,* 37 USPQ2d 1578, 1581, 76 F.3d 1168, 1172 (Fed. Cir. 1996), quoting Vas-Cath Inc. v. Mahurkar 935 F.2d 1563-1564, 19 USPQ 1111, 1117 (Fed. Cir. 1991).

Based on data provided in the application, the skilled artisan would expect a polypeptide of SEQ ID NO: 1 to provide protection against at least *S. aureus* COL and strains having a sai-1 sequence with a degree of sequence similarity to the *S. aureus* COL sequence. SEQ ID NO: 1 was obtained by making certain modifications to the naturally occurring COL sequence provided by SEQ ID NO: 7. (See for example, Figure 1 illustrating SEQ ID NO: 1 and Figure 3 illustrating SEQ ID NO: 3 and SEQ ID NO: 7. As noted above, SEQ ID NO: 3 is a His-Tag version of SEQ ID NO: 1.)

Claims 28-31 are composition claims specifically referring to the ability of the polypeptide immunogen to provide protection against *S. aureus* COL. The patent office has failed to provide a rationale as why a significant number of polypeptides generally covered by the claims would not provide production against *S. aureus* COL.

35 U.S.C. § 112, First Paragraph (New Matter): Claims 1-3, 5-7, and 19-31

Claims 1-3, 5-7 and 19-31 stand rejected as allegedly providing matter not described in the application. The rejection alleges the application fails to provide support for "consisting of an amino acid sequence of SEQ ID NO: 1 or a sequence that differs from SEQ ID NO: 1 by up to 15 amino acid alterations, . . wherein said polypeptide immunogen provides protective immunity against *S. aureus*". The rejection is respectfully traversed.

The provided "new matter" rejection appears to be the same rejection as the written description rejection addressed above. The office action does not assert the specification fails to recite elements in the claims as described in the specification. Instead, the present rejection, as with the previous rejection, appears to argue that the specification fails to show possession of a sequence differing from SEQ ID NO: 1 by up to 15 amino acids alterations able to provide protection against any strain or isolate of *S. aureus*.

To the extent the rejection is based on support in the application for the elements described in the claims, the application at page 2 refers to polypeptide immunogens comprising an amino acid sequence at least 85% identical to SEQ ID NO 1, where the polypeptide provides protective immunity against *S. aureus*. The application goes to provide written description support for limitations provided in the claims by further describing the polypeptide, for example:

> A polypeptide at least 85% identical to SEQ ID NO: 1 contains up to 26 amino acid alterations from SEQ ID NO: 1. SEQ ID NO: 2 is an example of a polypeptide structurally related to SEQ ID NO: 1. In different embodiments, the SEQ ID NO: 1 related polypeptide is at 90%, least 94%, or at least 99% identical to SEQ ID NO: 1; at least 94% or 99% identical to SEQ ID NO: 2; differs from SEQ ID NO: 1 or SEQ ID NO: 2 by 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid alterations; or consists essentially of amino acids 3-260 of SEQ ID NO: 1 or 3-264 of SEQ ID NO: 2. Each amino acid alteration is independently an addition, deletion or substitution.

(The application at page 7, second full paragraph.)

To the extent the rejection is based on the argument that the application allegedly does not provide written description support for scope of the claims, as discussed in the response to the § 112 (Written Description) rejection *supra*. the ability of SEQ ID NO: 3 to provide for protective immunity reasonably conveys to those skilled in the art that applicants were in possession of polypeptides having a substantially similar sequence to SEQ ID NO: 1 that provide protective immunity against *S. aureus*. The reasonable conveyance is provided by the high degree of structural relationship between the SEQ ID NO: 1 related polypeptides recited in the claims.

Because of the high degree of structural similarity for the polypeptide described in the claims and SEQ ID NO: 1, SEQ ID NO: 1 is sufficiently representative. Polypeptides having a high degree of structural similarity are expected to have similar properties. The rejected claims

provide for varying high degrees of structural similarity ranging from SEQ ID NO: 1 to 1-15 amino acid alterations.

The rejection ignores the structurally similarity of the polypeptides recited in the claims based on the potential alterations to critical amino acids impacting a protein antibody interaction. The rejection fails to provide any indication as to the probability that any particular amino acid alterations will likely prevent the SEQ ID NO: 1 from providing protective immunity.

35 U.S.C. § 112, First Paragraph (New Matter): Claim 5 and dependent claims

Claim 5 stands rejected as allegedly containing subject matter not described in the specification is such a way to reasonably convey to the skilled artisan the inventor at the time the invention was filed possessed the claimed invention. The rejection is directed to reference in the claim to "wherein said sai-1 region is present on a sequence found in a *S. aureus* sequence". The office action indicates that the specification at page 6, fourth paragraph, does not provide support for a sai-l region of microbial or non-microbial original present "on" a sequence found "in" a *S. aureus* sequence as recited. The rejection is respectfully traversed.

The objected to phrase is directed to a naturally occurring *S. aureus* sai-1 polypeptide region. Reference to *S. aureus* indicates a sequence which is microbial origin (*i.e., S. aureus* origin).

As noted above, claim 5 was amended to more particularly reference the sai-1 region as a polypeptide. Support for the amendment is provided in specification as follows:

> Reference to "additional region or moiety" indicates a region or moiety different from a sai-1 region. The additional region or moiety can be, for example, an additional polypeptide region or a non-peptide region.

(The specification at page 3, second paragraph.)

> Different sai-1 sequences may be present in different strains of *S.* aureus. Two examples of sai-1 sequences are provided by SEQ ID NO: 7 and 8. Other naturally occurring sai-1 sequences can be identified based on the presence of a high degree of sequence similarity or contiguous amino acids compared to a known sai-1 sequence. Contiguous amino acids provide characteristic tags. In different embodiments, a naturally occurring sai-1 sequence is a sequence found in a *Staphylococcus*, preferably *S. aureus,* having at least 20, at least 30, or at least 50 contiguous amino acids as in SEQ ID NO: 1; and/or having at least 85% sequence similarity or identity with SEQ ID NO: 1.

(The specification at page 6, fourth paragraph.) SEQ ID NOs: 7 and 8 are polypeptides.

35 U.S.C. § 112, Second Paragraph (Claims 3-7, 24, 29 and 31)

Claims 3, 24 and 31 stand rejected based on reference to "consisting essentially of". These claims were amended to replace reference to "consisting essentially" with "consists" of an indicated amino acid sequence and up to 15 amino acids at the carboxyl or amino terminus.

Claim 5 was indicated to be confusing based on reference to "sai-1 region is present on a sequence found in a *S. aureus* sequence". The rejection indicates is not clear whether sai-1 region is a non-peptide or non-protein region that is present "on" a nucleotide sequence found "in" a *S. aureus* protein or nucleotide sequence. Claim 5 was amended to more particularly point out that the referred to sai-1 region is present in a naturally occurring *S. aureus* polypeptide.

Claim 5 was indicated to be indefinite based on reference to "an" prior to sai-1. Claim 5 was amended as suggested by the examiner to indicate "a" prior sai-1.

Claim 29 was indicated to be incorrect based on reference to "by with". Claim 29 was amended to change "by with" to "with".

35 U.S.C. § 102 (Granoff et al.)

Claims 1, 5-7, 19, 21-23 and 26-30 stand rejected as allegedly anticipated by Granoff et al. (US 7,534,444) ('444). The rejection is based on the presence of a QTP region in SEQ ID NO: 1 and in polypeptides described in Granoff et al. ('444). The rejection is respectfully traversed.

The sequences referenced in Granoff et al. are not SEQ ID NO: 1, and differ from SEQ ID NO: 1 by more the number of amino acids differences mentioned in the rejected claims. The office action appears to point to only a three amino acid overlap.

Please charge deposit account 13-2755 for fees due in connection with this amendment. If any time extensions are needed for the timely filing of the present amendment, applicants petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

By /Sheldon O. Heber, Reg. No. 38,179/
Sheldon O. Heber
Reg. No. 38,179
Attorney for Applicants

Merck & Co., Inc.
P.O. Box 2000
Rahway, NJ 07065-0907
(732) 594-1958